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Communication

## On-resin peptide ligation *via* C-terminus benzyl ester

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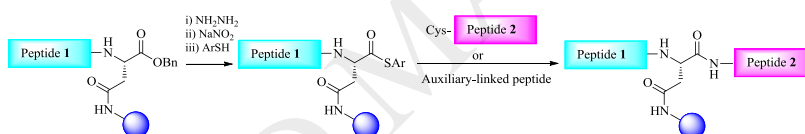
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### Graphical Abstract



Here, we reported a new approach of on-resin peptide ligation using C-terminal benzyl ester as the stabilized precursor of thioester, which enables both N-terminal elongation and C-terminal peptide ligation on a Rink Amide resin.

### ABSTRACT

Here, we report a new approach of on-resin peptide ligation using C-terminal benzyl ester as the stabilized precursor of thioester, which enables both N-terminal elongation and C-terminal peptide ligation on a Rink Amide resin. On-resin native chemical ligation and auxiliary-assisted peptide ligation were successfully achieved. This method is compatible to both protected and unprotected peptide fragments and has potential application in poor water-soluble peptide ligation.

Keywords:

On-resin peptide ligation

Peptide benzyl ester

Native chemical ligation

Auxiliary-assisted peptide ligation

Peptide elongation

Proteins and peptides are vital components of living organisms and play crucial roles in massive biological and physiological processes [1]. Solid phase peptide synthesis (SPPS) [2, 3] is widely applied in chemical synthesis of peptides and proteins after over 50-year development. For long peptides containing more than 50 amino acids in their sequences, native chemical ligation (NCL) [4-7] of two peptides was usually employed with C-terminal peptide thioesters and N-terminal cysteinyl peptides. Both Boc-protecting

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